



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/663,538

09/15/2003

Peter S. Lu

020054-000211US

5609

20350 7590 10/17/2007

TOWNSEND AND TOWNSEND AND CREW, LLP  
TWO EMBARCADERO CENTER  
EIGHTH FLOOR  
SAN FRANCISCO, CA 94111-3834

EXAMINER

BUNNER, BRIDGET E

ART UNIT

PAPER NUMBER

1647

MAIL DATE

DELIVERY MODE

10/17/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/663,538

Applicant(s)

LU ET AL.

Examiner

Bridget E. Bunner

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 02 August 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 7, 13, 14 and 18-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8-12 and 15-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-20 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 January 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Appendices A and B</u>                 |

## DETAILED ACTION

### *Status of Application, Amendments and/or Claims*

The amendment of 02 August 2007 has been entered in full. Claims 1, 2, 4, 6, 15 are amended.

This application contains claims 7, 13, 14, and 18-20 drawn to an invention nonelected with traverse in the reply filed on 20 November 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-6, 8-12, and 15-17 are under consideration in the instant application.

### *Withdrawn Objections and/or Rejections*

1. The objections to the specification at pages 4-5 of the previous Office Action (02 February 2007) are *withdrawn in part* in view of the amended specification (02 August 2007). Please see section on Specification, below.
2. The objections to claims 1-4, 6, and 15 at page 5 of the previous Office Action (02 February 2007) are *withdrawn in part* in view of the amended claims (02 August 2007). Please see section on Claim Objections, below.
3. The rejection of claims 1-3, 6, 8-12, and 15-17 under 35 U.S.C. § 112, first paragraph (scope of enablement) for recitation of nucleic acid variants as set forth at pages 12-14 of the previous Office Action (02 February 2007) is *withdrawn* in view of the amended claims (02 August 2007).

Art Unit: 1647

4. The rejection of claims 1-6, 8-12, and 15-17 under 35 U.S.C. § 112, first paragraph (written description) as set forth at pages 18-20 of the previous Office Action (02 February 2007) is *withdrawn* in view of the amended claims (02 August 2007).
5. The rejection of claim 5 under 35 U.S.C. § 112, first paragraph (Deposit Rules) as set forth at pages 20-22 of the previous Office Action (02 February 2007) is *withdrawn* in view of Applicant's declaration of 02 August 2007.
6. The rejection of claims 1-6, 8-12, and 15-17 under 35 U.S.C. § 112, second paragraph as set forth at page 22 of the previous Office Action (02 February 2007) is *withdrawn* in view of the amended claims (02 August 2007).
7. The rejection of claims 1, 15-16 under 36 U.S.C. § 102(b) as set forth at pages 22-23 of the previous Office Action (02 February 2007) is *withdrawn* in view of the amended claims (02 August 2007).
8. The rejection of claims 8-12 and 17 under 35 U.S.C. § 103(a) as set forth at pages 23-25 of the previous Office Action (02 February 2007) is *withdrawn* in view of the amended claims (02 August 2007).

#### ***Sequence Compliance***

The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (02 August 2007) has been considered and is found persuasive. Therefore, the requirements set forth in the Notice to Comply (02 February 2007) are *withdrawn*.

#### ***Specification***

9. The disclosure is objected to because of the following informalities:

Art Unit: 1647

9a. The specification refers to Figures which were deleted in the amendment of 16 January 2004. Please see, for example, pages 25, 45, 47, 68, 113, 114, 115, 125. The basis for this objection is set forth at page 4 of the previous Office Action (02 February 2007).

It is noted that at page 1 of the response of 02 August 2007, Applicant indicates that Applicant is reconsidering re-introducing these figures into the application.

Appropriate correction is required.

### ***Claim Objections***

10. Claims 4, 6 and 15 are objected to because of the following informalities:

10a. Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 (upon which claim 4 depends) and claim 4 both recite a polynucleotide encoding SEQ ID NO: 2.

10b. Claims 6 and 15 use the acronym "CLASP-2" without first defining what they represent in the independent claims. While the claims can reference acronyms, the material presented by the acronym must be clearly set forth at the first use of the acronym. The basis for this objection is set forth at page 5 of the previous Office Action (02 February 2007).

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 101 and § 112, first paragraph***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

Art Unit: 1647

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-6, 8-12, and 15-17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation. The basis for this rejection is set forth at pages 5-11 of the previous Office Action (02 February 2007).

Applicant's arguments (02 August 2007), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts at page 2 of the Response that knowledge of how an invention works is not needed for patentability. Applicant indicates that it is enough for Applicants to have identified that CLASP-2 is involved in such processes, and to have identified the disease states that ultimately correlate with CLASP-2 dysfunction.

Applicant's arguments have been fully considered but are not found to be persuasive. Although knowledge of how an invention works is not needed for patentability, the invention must be supported by either a credible, specific, and substantial asserted utility or a well established utility. In the instant application, the specification does not disclose any methods or working examples that indicate the CLASP-2 polynucleotide and polypeptide are involved in any processes, such as T cell activation, regulation of T cell and B cell interactions, and in the organization, establishment, and maintenance of the "immunological synapse" (including signal transduction, cytoskeletal interactions, and membrane organization) (pg 22, lines 1-7; pg 21, lines 1-5). Since significant further research would be required of the skilled artisan to determine

Art Unit: 1647

how the claimed polypeptide is involved with the above-mentioned activities, the asserted utilities are not substantial. Since the utility is not presented in mature form and significant further research is required, the utility is not substantial.

The specification also does not disclose any disease states associated with a mutated, deleted, or translocated CLASP-2 gene (SEQ ID NO: 1) or protein (SEQ ID NO: 2). The specification does not disclose which disorders are associated with altered levels of the CLASP-2 gene or protein. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

(ii) At page 3 of the Response, Applicant argues that post-filing date work has confirmed the involvement of CLASP-2 in immune response, especially T-cell activation. Applicant indicates that multiple publications have shown that CLASP-2 (called Zizimin 1 or DOCK9) interacts with and activates a rho-family GTPase called cdc42 (Meller et al. 2002). Applicant also submits that activated cdc42 promotes cytoskeletal polarization of T cells in response to contact with antigen-presenting cells (Stowers et al. 1995). Applicant concludes that the role of CLASP-2 in promoting T cell activation is of clear relevance to immunological diseases such as immune system disorders, allergic reactions, organ rejection, etc.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant indicates that CLASP-2 is also known as Zizimin 1 or DOCK9, which has been shown to interact with cdc42. However, according to the Examiner's sequence search of 18 December 2006, the CLASP-2 amino acid sequence of SEQ ID NO: 2 is only 94.0% identical to

Art Unit: 1647

Zizimin1/DOCK9 (see sequence alignment attached to the instant Office Action as Appendix A). Additionally, the CLASP-2 nucleic acid sequence of SEQ ID NO: 1 is only 73.8% identical to the Zizimin1 nucleic acid sequence (see sequence alignment attached to the instant Office Action as Appendix B). Thus, it is not clear how Applicant has concluded that CLASP-2 is Zizimin1/DOCK9. From the sequence search performed by the PTO, it seems that CLASP-2 and Zizimin1/DOCK9 are different proteins.

Additionally, although the specification of the instant application teaches that CLASP-2 expression levels decrease at 1 hour, 2 hours, and 4 hours after T cell activation (pg 125, lines 4-14), it cannot be determined if this decrease is a significant difference as compared to T-cells that have not been activated. If the decrease in CLASP-2 expression is not significant between the two cell types, then this utility is not specific because the skilled artisan would not be able to distinguish activated T-cells from inactivated T-cells. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. Applicant is encouraged to submit any evidence under 37 C.F.R. 1.132 that would indicate a significant difference between the expression of CLASP-2 in activated and inactivated T-cells.

(iii) At the bottom of page 3 of the Response, Applicant contends that the very striking similarity between CLASP-1 and CLASP-2 (Figure 5) imparts substantial credibility to Applicant's assertion that CLASP-2 (like CLASP-1) is involved in T-cell activation. Applicant asserts that there is no basis for the Examiner to argue to the contrary or to assert that Applicant's disclosed utility of CLASP-2 is neither specific nor substantial.



Applicant's arguments have been fully considered but are not found to be persuasive.

The truth, or credibility, of the assertion of utility has not been questioned. Rather, the rejection sets forth that the assertion of utility is not specific or substantial. In the previous Office Action of 02 February 2007, the Examiner made a *prima facie* showing that the claimed invention lacks utility and provided sufficient evidentiary basis for factual assumptions relied upon in establishing the *prima facie* showing. The assertion that the disclosed CLASP-2 polynucleotide has biological activities similar to protein family members having a role in T cell activation is not specific or substantial in the absence of supporting evidence, because the relevant literature reports numerous examples of polypeptide families wherein individual members have distinct, and even opposite, biological activities. For example, Tischer et al. (U.S. Patent 5,194,596) establishes that VEGF (a member of the PDGF, or platelet-derived growth factor, family) is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of naturally occurring PDGF which is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). The differences between PDGF and VEGF are also seen *in vivo*, wherein endothelial-pericyte associations in the eye are disrupted by intraocular administration of PDGF but accelerated by intraocular administration of VEGF (Benjamin et al., 1998, Development 125:1591-1598; see Abstract and pp. 1594-1596). Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF- $\beta$  family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF- $\beta$  family members BMP-2 and TGF- $\beta$ 1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). See also Massague, who reviews other members of the TGF- $\beta$  family (1987, Cell 49:437-8, esp. p.

Art Unit: 1647

438, column 1, second full paragraph to the end). Similarly, PTH and PTHrP are two structurally closely related proteins which can have opposite effects on bone resorption (Pilbeam et al., 1993, Bone 14:717-720; see p. 717, second paragraph of Introduction). Finally, Kopchick et al. (U.S. Patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid (column 2, lines 37-48). Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different

Art Unit: 1647

molecular and cellular functions. Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. Thus, the specification fails to support the asserted credible, specific and substantial utility of T cell activation.

(iv) At page 4 of the Response, Applicant argues that the Office Action's allegation that it is necessary to completely characterize the nature of CLASP-2's involvement in T cell activation is incorrect. Applicant adds that inhibitors can be identified by the relatively simple *in vitro* binding assays disclosed in the specification. Applicant states that it is not necessary to have a complete understanding of underlying mechanisms to identify inhibitors of CLASP-2 activity, nor to perform trials of such identified inhibitors in cellular or animal models for activity in protecting against cell death. Applicant indicates that usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development and cites *in re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995).

Applicant's arguments have been fully considered but are not found to be persuasive. The asserted utilities put forth by Applicant and the specification of the instant application are credible, but not specific or substantial. The asserted utility of screening for activators/inhibitors can be performed with any polypeptide. The specification also discloses nothing specific or substantial about the ligands, agonists/antagonists, and binding proteins that are identified by these methods. Substantial further research is required to determine the usefulness of agonists,

Art Unit: 1647

antagonists isolated in this manner. Since these asserted utilities are also not present in mature form, so that they could be readily used in a real world sense, the asserted utilities are not substantial. Furthermore, the fact patterns of the case cited by the Applicant and of the instant rejection are significantly different, and the court decision is not binding with regard to the instant rejection. Although, as discussed *in re Brana*, that pharmaceutical inventions necessarily include further research and development, it is clear from the instant specification that the polypeptide described therein is what is termed an “orphan protein” in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this DNA and protein, may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are “useful” to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of “useful” as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed “real world” utility.

12. Claims 1-6, 8-12, and 15-17 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial

Art Unit: 1647

asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at pages 11-12 of the previous Office Action (02 February 2007).

Applicant's arguments (02 August 2007), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant states that a specific and substantial asserted utility, as described above. Specifically, since Applicant has not provided evidence to demonstrate that the CLASP-2 polynucleotide and polypeptide have a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention. It is noted that the instant specification is required to teach one skilled in the art how to make and use the polypeptide encoded by the claimed polynucleotides.

13. However, even if the claimed invention is eventually deemed to have a credible, specific and substantial asserted utility or a well established utility, claims 10-12 would remain rejected under 35 U.S.C. § 112, first paragraph. The basis for this issue is set forth at pages 14-17 of the previous Office Action (02 February 2007) and is reiterated herein below.

The Examiner has interpreted claims 10-12 as reading on isolated host cells, as well as host cells in the context of a multicellular, transgenic organism and host cells intended for gene therapy. The specification of the instant application teaches that CLASP-2 gene can be expressed in transgenic animals and any technique known in the art may be used to introduce a CLASP-2 transgene into animals to produce the founder lines of transgenic animals (pg 66-67). However, there are no methods or working examples disclosed in the instant application whereby

Art Unit: 1647

a multicellular animal with the incorporated CLASP-2 gene of SEQ ID NO: 1 is demonstrated to express the CLASP-2 peptide. There are also no methods or working examples in the specification indicating that a multicellular animal has CLASP-2 "knocked out". The unpredictability of the art is *very high* with regards to making transgenic animals. For example, Wang et al. (Nuc. Acids Res. 27: 4609-4618, 1999; pg 4617) surveyed gene expression in transgenic animals and found in each experimental animal with a single "knock-in" gene, multiple changes in genes and protein products, often many of which were unrelated to the original gene. Likewise, Kaufman et al (Blood 94: 3178-3184, 1999) found transgene expression levels in their transfected animals varied from "full" (9 %) to "intermediate" to "none" due to factors such as "vector poisoning" and spontaneous structural rearrangements (pg 3180, col 1, 2<sup>nd</sup> full paragraph; pg 3182-3183). Additionally, for example, the specification discloses that two possible techniques used to introduce a CLASP-2 transgene into animals include pronuclear microinjection and gene targeting in embryonic stem cells (pg 66, lines 28-31). However, the literature teaches that the production of transgenic animals by microinjection of embryos suffers from a number of limitations, such as the extremely low frequency of integration events and the random integration of the transgene into the genome which may disrupt or interfere with critical endogenous gene expression (Wigley et al. Reprod Fert Dev 6: 585-588, 1994). The inclusion of sequences that allow for homologous recombination between the transgenic vector and the host cell's genome does not overcome these problems, as homologous recombination events are even rarer than random events. Therefore, in view of the extremely low frequency of both targeted and non-targeted homologous recombination events in microinjected embryos, it would have required undue experimentation for the skilled artisan to have made any and all transgenic

non-human animals according to the instant invention. Furthermore, regarding gene targeting in embryonic stem cells, the specification does not provide guidance for identifying and isolating embryonic stem cells or for identifying other embryonal cells which are capable of contributing to the germline of any animal. At the time of filing, Campbell et al. teaches that, "in species other than the mouse the isolation of ES cells has proved more difficult. There are reports of ES-like cell lines in a number of species...However, as yet there are not reports of any cell lines which contribute to the germ line in any species other than mouse" (Campbell et al. Theriology 47(1): 63-72, 1997; see pg 65, 2<sup>nd</sup> paragraph). Thus, based on the art recognized unpredictability of isolating and using embryonic stem cells or other embryonal cells from animals other than mice to produce transgenic animals, and in view of the lack of guidance provided by the specification for identifying and isolating embryonal cells which can contribute to the germ line of any non-human mammal other than the mouse, such as dogs or cows, the skilled artisan would not have had a reasonable expectation of success in generating any and all non-human transgenic animals using ES cell technology.

The specification also discloses that nucleic acids encoding the CLASP-2 polypeptide can be used for gene therapy (pg 62-65). However, the specification does not teach any methods or working examples that indicate a CLASP-2 nucleic acid is introduced and expressed in a cell for therapeutic purposes. The disclosure in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. For example, the specification does not teach what type of vector would introduce the CLASP-2 nucleic acid into the cell or in what quantity and duration. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has

Art Unit: 1647

been seen, it has generally been inadequate for a meaningful clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must be designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be required of the skilled artisan to introduce and express a CLASP2 nucleic acid into the cell of an organism.

Additionally, gene therapy is unpredictable and complex wherein one skilled in the art may not necessarily be able to introduce and express a CLASP-2 nucleic acid in the cell of an organism or be able to produce a CLASP-2 protein in that cell. (Please note that this issue could be overcome by amending the claims to recite, for example, "An isolated host cell...").

Due to the large quantity of experimentation necessary to generate a transgenic animal expressing the CLASP-2 protein and to introduce and express a CLASP-2 nucleic acid in a cell of an organism for therapy; the lack of direction/guidance presented in the specification regarding how to introduce a CLASP-2 nucleic acid in the cell of an organism to be able produce that CLASP-2; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art which establishes the unpredictability of making transgenic animals and of transferring genes into an organism's cells; and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.



Art Unit: 1647

***Conclusion***

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

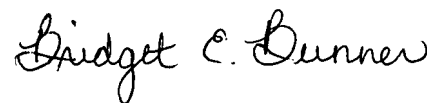
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB  
Art Unit 1647  
12 October 2007



BRIDGET E. BUNNER  
PRIMARY EXAMINER

## Appendix A

```

<!--StartFragment-->RESULT 3
DOCK9_HUMAN
ID DOCK9_HUMAN STANDARD; PRT; 2069 AA.
AC Q9BZ29; Q5JUD4; Q5JUD6; Q5T2Q1; Q5TAN8; Q9BZ25; Q9BZ26; Q9BZ27;
AC Q9BZ28; Q9UPU4;
DT 19-OCT-2002, integrated into UniProtKB/Swiss-Prot.
DT 19-OCT-2002, sequence version 2.
DT 07-MAR-2006, entry version 39.
DE Deducator of cytokinesis protein 9 (Cdc42 guanine nucleotide exchange
DE factor zizimin 1).
GN Name=DOCK9; Synonyms=KIAA1058;
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC Homo.
OX NCBI_TaxID=9606;
RN [1]
RP NUCLEOTIDE SEQUENCE (ISOFORM 1), FUNCTION, INTERACTION WITH CDC42, GEF
RP ACTIVITY, AND TISSUE SPECIFICITY.
RX MEDLINE=22194783; PubMed=12172552; DOI=10.1038/ncb835;
RA Meller N., Irani-Tehrani M., Kiosses W.B., Del Pozo M.A.,
RA Schwartz M.A.;
RT "Zizimin1, a novel Cdc42 activator, reveals a new GEF domain for Rho
RT proteins.";
RL Nat. Cell Biol. 4:639-647(2002).
RN [2]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM 2).
RC TISSUE=Brain;
RX MEDLINE=99397452; PubMed=10470851; DOI=10.1093/dnares/6.3.197;
RA Kikuno R., Nagase T., Ishikawa K., Hirose M., Miyajima N.,
RA Tanaka A., Kotani H., Nomura N., Ohara O.;
RT "Prediction of the coding sequences of unidentified human genes. XIV.
RT The complete sequences of 100 new cDNA clones from brain which code
RT for large proteins in vitro.";
RL DNA Res. 6:197-205(1999).
RN [3]
RP SEQUENCE REVISION.
RX MEDLINE=22158633; PubMed=12168954; DOI=10.1093/dnares/9.3.99;
RA Nakajima D., Okazaki N., Yamakawa H., Kikuno R., Ohara O., Nagase T.;
RT "Construction of expression-ready cDNA clones for KIAA genes: manual
RT curation of 330 KIAA cDNA clones.";
RL DNA Res. 9:99-106(2002).
RN [4]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA] (ISOFORMS 1; 2; 3 AND
RP 4).
RX PubMed=15057823; DOI=10.1038/nature02379;
RA Dunham A., Matthews L.H., Burton J., Ashurst J.L., Howe K.L.,
RA Ashcroft K.J., Beare D.M., Burford D.C., Hunt S.E.,
RA Griffiths-Jones S., Jones M.C., Keenan S.J., Oliver K., Scott C.E.,
RA Ainscough R., Almeida J.P., Ambrose K.D., Andrews D.T.,
RA Ashwell R.I.S., Babbage A.K., Bagguley C.L., Bailey J., Bannerjee R.,
RA Barlow K.F., Bates K., Beasley H., Bird C.P., Bray-Allen S.,
RA Brown A.J., Brown J.Y., Burrill W., Carder C., Carter N.P.,
RA Chapman J.C., Clamp M.E., Clark S.Y., Clarke G., Clee C.M.,
RA Clegg S.C., Copley V., Collins J.E., Corby N., Coville G.J.,
RA Deloukas P., Dhami P., Dunham I., Dunn M., Earthrowl M.E.,
RA Ellington A.G., Faulkner L., Frankish A.G., Frankland J., French L.,
RA Garner P., Garnett J., Gilbert J.G.R., Gilson C.J., Ghori J.,
RA Grafham D.V., Gribble S.M., Griffiths C., Hall R.E., Hammond S.,
RA Harley J.L., Hart E.A., Heath P.D., Howden P.J., Huckle E.J.,
RA Hunt P.J., Hunt A.R., Johnson C., Johnson D., Kay M., Kimberley A.M.,
RA King A., Laird G.K., Langford C.J., Lawlor S., Leongamornlert D.A.,
RA Lloyd D.M., Lloyd C., Loveland J.E., Lovell J., Martin S.,
RA Mashregi-Mohammadi M., McLaren S.J., McMurray A., Milne S.,
RA Moore M.J.F., Nickerson T., Palmer S.A., Pearce A.V., Peck A.I.,
RA Pelan S., Phillimore B., Porter K.M., Rice C.M., Searle S.,
RA Sehra H.K., Shownkeen R., Skuce C.D., Smith M., Steward C.A.,
RA Sycamore N., Tester J., Thomas D.W., Tracey A., Tromans A., Tubby B.,
RA Wall M., Wallis J.M., West A.P., Whitehead S.L., Willey D.L.,
RA Wilming L., Wray P.W., Wright M.W., Young L., Coulson A., Durbin R.,
RA Hubbard T., Sulston J.E., Beck S., Bentley D.R., Rogers J., Ross M.T.;
RT "The DNA sequence and analysis of human chromosome 13.";
RL Nature 428:522-528(2004).
RN [5]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] OF 1551-2069 (ISOFORM 4).
RC TISSUE=Eye;

```

Appendix A

RX MEDLINE=22388257; PubMed=12477932; DOI=10.1073/pnas.242603899;  
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,  
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,  
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,  
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,  
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,  
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,  
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,  
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,  
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,  
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,  
 RA Villalón D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,  
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,  
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,  
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,  
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,  
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,  
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;  
 RT "Generation and initial analysis of more than 15,000 full-length human  
 RT and mouse cDNA sequences.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).  
 RN [6]  
 RP NOMENCLATURE, AND GEF ACTIVITY.  
 RX MEDLINE=22319137; PubMed=12432077; DOI=10.1242/jcs.00219;  
 RA Cote J.-F., Vuori K.;  
 RT "Identification of an evolutionarily conserved superfamily of DOCK180-  
 RT related proteins with guanine nucleotide exchange activity.";  
 RL J. Cell Sci. 115:4901-4913(2002).  
 CC -!- FUNCTION: Guanine nucleotide-exchange factor (GEF) that activates  
 CC CDC42 by exchanging bound GDP for free GTP. Overexpression induces  
 CC filopodia formation.  
 CC -!- SUBUNIT: Interacts preferentially with nucleotide-depleted CDC42.  
 CC -!- SUBCELLULAR LOCATION: Cytoplasmic; associated with membranes  
 CC (Probable).  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event=Alternative splicing; Named isoforms=4;  
 CC Name=1;  
 CC IsoId=Q9BZ29-1; Sequence=Displayed;  
 CC Name=2;  
 CC IsoId=Q9BZ29-5; Sequence=VSP\_017128;  
 CC Name=3;  
 CC IsoId=Q9BZ29-3; Sequence=VSP\_004024;  
 CC Note=No experimental confirmation available;  
 CC Name=4;  
 CC IsoId=Q9BZ29-4; Sequence=VSP\_007709, VSP\_007710;  
 CC Note=Produced by exon skipping that results in a frameshift. No  
 CC experimental confirmation available;  
 CC -!- TISSUE SPECIFICITY: Widely expressed, with highest expression in  
 CC heart and placenta. Expressed at intermediate level in kidney,  
 CC brain, lung and skeletal muscle.  
 CC -!- DOMAIN: The DHR-2 domain is necessary and sufficient for the GEF  
 CC activity.  
 CC -!- MISCELLANEOUS: 'Zizim' means 'spike' in Hebrew.  
 CC -!- SIMILARITY: Belongs to the DOCK family.  
 CC -!- SIMILARITY: Contains 1 DHR-1 (CZH-1) domain.  
 CC -!- SIMILARITY: Contains 1 DHR-2 (CZH-2) domain.  
 CC -!- SIMILARITY: Contains 1 PH domain.  
 CC -----  
 CC Copyrighted by the UniProt Consortium, see <http://www.uniprot.org/terms>  
 CC Distributed under the Creative Commons Attribution-NoDerivs License  
 CC -----  
 DR EMBL; AF527605; AAM90306.1; -; mRNA.  
 DR EMBL; AB028981; BAA83010.2; ALT INIT; mRNA.  
 DR EMBL; AL139084; CAI13370.1; -; Genomic\_DNA.  
 DR EMBL; AL161420; CAI13370.1; JOINED; Genomic\_DNA.  
 DR EMBL; AL139084; CAI13372.1; -; Genomic\_DNA.  
 DR EMBL; AL161420; CAI13372.1; JOINED; Genomic\_DNA.  
 DR EMBL; AL391122; CAI13372.1; JOINED; Genomic\_DNA.  
 DR EMBL; AL161420; CAI39569.1; -; Genomic\_DNA.  
 DR EMBL; AL139084; CAI39569.1; JOINED; Genomic\_DNA.  
 DR EMBL; AL161420; CAI39570.1; -; Genomic\_DNA.  
 DR EMBL; AL161420; CAI39574.1; -; Genomic\_DNA.  
 DR EMBL; AL139084; CAI39574.1; JOINED; Genomic\_DNA.  
 DR EMBL; AL391122; CAI39574.1; JOINED; Genomic\_DNA.  
 DR EMBL; AL161420; CAI39577.1; -; Genomic\_DNA.  
 DR EMBL; AL391122; CAI11061.1; -; Genomic\_DNA.

Appendix A

DR EMBL; AL139084; CAI11061.1; JOINED; Genomic\_DNA.  
 DR EMBL; AL161420; CAI11061.1; JOINED; Genomic\_DNA.  
 DR EMBL; BC043506; AAH43506.1; -; mRNA.  
 DR PDB; 1WG7; NMR; A=165-301.  
 DR Ensembl; ENSG00000088387; Homo sapiens.  
 DR HGNC; HGNC:14132; DOCK9.  
 DR MIM; 607325; gene.  
 DR LinkHub; Q9BZ29; -.  
 DR InterPro; IPR010703; DOCK.  
 DR InterPro; IPR001849; PH.  
 DR InterPro; IPR011993; PH\_type.  
 DR Pfam; PF06920; Ded\_cyto; 1.  
 DR Pfam; PF00169; PH; 1.  
 DR SMART; SM00233; PH; 1.  
 DR PROSITE; PS50003; PH\_DOMAIN; 1.  
 KW 3D-structure; Alternative splicing; Coiled coil;  
 KW Guanine-nucleotide releasing factor; Repeat.  
 FT CHAIN 1 2069 Dedicator of cytokinesis protein 9.  
 FT /FTid=PRO\_0000189999.  
 FT DOMAIN 174 281 PH.  
 FT DOMAIN 641 879 DHR-1.  
 FT DOMAIN 1505 2060 DHR-2.  
 FT COILED 1948 1982 Potential.  
 FT COILED 2034 2067 Potential.  
 FT VARSPLIC 1 43 MSQPPELLPASAETRKFTALSKPGTAAELRQSVSEVVRGSV  
 FT LL -> MQADKCRITSSRSVKELVIESPLQYKDAAQGEVEA  
 FT ESPGPVP (in isoform 2).  
 FT /FTid=VSP\_017128.  
 FT VARSPLIC 1355 1378 RTGMMHARLQQLGSLDNSLTFNHS -> SVRKISSVLGISV  
 FT DNG (in isoform 3).  
 FT /FTid=VSP\_004024.  
 FT VARSPLIC 1791 1804 Missing (in isoform 4).  
 FT /FTid=VSP\_007709.  
 FT VARSPLIC 2068 2069 LG -> ICPLEEKTSVLPNSLHIFNAISGTPSTMTVMHGMTS  
 FT SSSVV (in isoform 4).  
 FT /FTid=VSP\_007710.  
 FT STRAND 170 170  
 FT STRAND 172 172  
 FT STRAND 178 183  
 FT STRAND 188 189  
 FT HELIX 190 194  
 FT STRAND 195 196  
 FT STRAND 198 206  
 FT STRAND 208 210  
 FT STRAND 212 220  
 FT STRAND 223 224  
 FT STRAND 227 230  
 FT TURN 232 234  
 FT STRAND 237 238  
 FT STRAND 243 244

Query Match 94.0%; Score 6584.5; DB 1; Length 2069;  
 Best Local Similarity 92.4%; Pred. No. 0;  
 Matches 1285; Conservative 2; Mismatches 3; Indels 101; Gaps 3;

Qy 1 VLHHHQNPPEFYDEIKIELPTQLHEKHLLLTFFHVSCDNSSKGSTKKRDVVETQVGYSWL 60  
 Db 701 VLHHHQNPPEFYDEIKIELPTQLHEKHLLLTFFHVSCDNSSKGSTKKRDVVETQVGYSWL 760  
 Qy 61 PLLKDGRVVTSEQHIPVSANLPSGYLGQELGMGRHYGPEIKWVDGGKPLLKISTHLVST 120  
 Db 761 PLLKDGRVVTSEQHIPVSANLPSGYLGQELGMGRHYGPEIKWVDGGKPLLKISTHLVST 820  
 Qy 121 VYTQDQHLHNFQYQCQKTESGAQALGNELVKYLSLHAMEGHVMIAFLPTILNQLFRVLT 180  
 Db 821 VYTQDQHLHNFQYQCQKTESGAQALGNELVKYLSLHAMEGHVMIAFLPTILNQLFRVLT 880  
 Qy 181 RATQEEVAVNVTRVIIHVVAQCHEEGLESHLSYVKYAYKAEPYVASEYKTVHEELTKSM 240  
 Db 881 RATQEEVAVNVTRVIIHVVAQCHEEGLESHLSYVKYAYKAEPYVASEYKTVHEELTKSM 940  
 Qy 241 TTILKPSADFLTSNKLRLYSWFFFDVLIKSMAQHLENSKVKLLRNQRFPPASYHHAETV 300  
 Db 941 TTILKPSADFLTSNKLRLYSWFFFDVLIKSMAQHLENSKVKLLRNQRFPPASYHHAETV 1000  
 Qy 301 VNMLMPHITQKFGDNPEASKNANHS LAVFIKRCFTFMDRGFVFKQINNYISCFAPGDPKT 360

Appendix A

```

Db      1001  VNMMLPHITQKFRDNPEASKNANHSLAVFIKRCFTFMDRGFVFKQINNYISCFAPGDPKT 1060
Qy      361  LFEYKFEFLRVVCNHEHYIPLNLPMFPGKGRIQRYQDLQLDYSLTDEFCRNHFLVGLLLR 420
Db      1061  LFEYKFEFLRVVCNHEHYIPLNLPMFPGKGRIQRYQDLQLDYSLTDEFCRNHFLVGLLLR 1120
Qy      421  EVGTALQEFREVRLIAISVLKNLLIKHSFDDRYASRSHQARIATLYLPLFGLLIENVQRI 480
Db      1121  EVGTALQEFREVRLIAISVLKNLLIKHSFDDRYASRSHQARIATLYLPLFGLLIENVQRI 1180
Qy      481  NVRDVSFPFVNAGMTVKDESALPAVNPLVTPQKGSTLDNSLHKDLLGAISGIASPYTTS 540
Db      1181  NVRDVSFPFVNAGMTVKDESALPAVNPLVTPQKGSTLDNSLHKDLLGAISGIASPYTTS 1240
Qy      541  TPNINSVRNADSRGSLISTDSGNSLPERNSEKSNSLDKHQSSSTLGNSVVRCDKLDQSEI 600
Db      1241  TPNINSVRNADSRGSLISTDSGNSLPERNSEKSNSLDKHQSSSTLGNSVVRCDKLDQSEI 1300
Qy      601  KSLLMCFLYILKMSDDALFTYWNKASTSELMDFFTISEVCLHQFYMGKRYIARNQEGL 660
Db      1301  KSLLMCFLYILKMSDDALFTYWNKASTSELMDFFTISEVCLHQFYMGKRYIA----- 1354
Qy      661  GPIVHDRKSQTLPVSRNRTGMMHARLQQLGSLDNLSTFNHSGHSDADVLHQSLEANIA 720
Db      1355  -----RTGMMHARLQQLGSLDNLSTFNHSGHSDADVLHQSLEANIA 1397
Qy      721  TEVCLTALDTLSLFTLAFKNQLLADHGHNPLMKKVFDVYLCFLQKHQSETALKNVFTALR 780
Db      1398  TEVCLTALDTLSLFTLAFKNQLLADHGHNPLMKKVFDVYLCFLQKHQSETALKNVFTALR 1457
Qy      781  SLIYKFPSTFYEGRADMCAALCYEILKCCNSKLSSIRTEASQLLYFLMRNNFDYTGKKSF 840
Db      1458  SLIYKFPSTFYEGRADMCAALCYEILKCCNSKLSSIRTEASQLLYFLMRNNFDYTGKKSF 1517
Qy      841  VRTHLQVIISVSQLIADVVGIGETRFFQQSLSIINNCCANSRDLIKHTSFSSDVKDLTKRIR 900
Db      1518  VRTHLQVIISVSQLIADVVGIGETRFFQQSLSIINNCCANSRDLIKHTSFSSDVKDLTKRIR 1577
Qy      901  TVLMATAQMKHEHNDPEMLVDLQYSLAKSYASTPELRKTWLDSMARIHVKNGLSEAAMC 960
Db      1578  TVLMATAQMKHEHNDPEMLVDLQYSLAKSYASTPELRKTWLDSMARIHVKNGLSEAAMC 1637
Qy      961  YVHVTALVAEYLTRK-----GVFRQGCTAFRVITPNIDEAS 997
Db      1638  YVHVTALVAEYLTRKEAVQWEPPLPHSHSACLRRSRGGVFRQGCTAFRVITPNIDEAS 1697
Qy      998  MMEDVGMQDVHFNEDVLMELLEQCADGLWKAERYELIADYKLIPIYEKRRD----- 1050
Db      1698  MMEDVGMQDVHFNEDVLMELLEQCADGLWKAERYELIADYKLIPIYEKRRDFERLAHL 1757
Qy      1051  -----FFEDEDGKEYIY 1062
Db      1758  YDTLHRAYSKVTEVMHSGRLLGTYFRVAFFGQAAQYQFTDSETDVEGFFEDEDGKEYIY 1817
Qy      1063  KEPKLTPLSEISQRLKLYSDKFGSENVKMIQDSGKVNPKDLDSKYAYIQVTHVIPFFDE 1122
Db      1818  KEPKLTPLSEISQRLKLYSDKFGSENVKMIQDSGKVNPKDLDSKYAYIQVTHVIPFFDE 1877
Qy      1123  KELQERKTEFERSHNIRRFMFEMPFTQTGKRQGGVEEQCKRRTILTAIHCFPYVKRIPV 1182
Db      1878  KELQERKTEFERSHNIRRFMFEMPFTQTGKRQGGVEEQCKRRTILTAIHCFPYVKRIPV 1937
Qy      1183  MYQHHTDLNPIEVAIDEMSKKVAELRQLCSSAEVDMIKLQLKQGSVSVQVNAGPLAYAR 1242
Db      1938  MYQHHTDLNPIEVAIDEMSKKVAELRQLCSSAEVDMIKLQLKQGSVSVQVNAGPLAYAR 1997
Qy      1243  AFLDDTNTKRYPDNKVKLLKEVFRQFVEACGQALAVNERLIKEDQLEYQEEMKANYREMA 1302
Db      1998  AFLDDTNTKRYPDNKVKLLKEVFRQFVEACGQALAVNERLIKEDQLEYQEEMKANYREMA 2057
Qy      1303  KELSEIMHEQI 1313
Db      2058  KELSEIMHEQL 2068

```

&lt;!--EndFragment--&gt;

Appendix B

```

<!--StartFragment-->RESULT 2
DQ047772
LOCUS      DQ047772          6195 bp    DNA        linear    GSS 02-JUN-2005
DEFINITION Homo sapiens ZIZIMIN1 gene, VIRTUAL TRANSCRIPT, partial sequence,
            genomic survey sequence.
ACCESSION  DQ047772
VERSION    DQ047772.1  GI:66900971
KEYWORDS   GSS.
SOURCE     Homo sapiens (human)
ORGANISM   Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE  1 (bases 1 to 6195)
AUTHORS    Nielsen,R., Bustamante,C., Clark,A.G., Glanowski,S., Sackton,T.B.,
            Hubisz,M.J., Fledel-Alon,A., Tanenbaum,D.M., Civello,D.,
            White,T.J., Sninsky,J.J., Adams,M.D. and Cargill,M.
TITLE      A Scan for Positively Selected Genes in the Genomes of Humans and
            Chimpanzees
JOURNAL    (er) PLoS Biol. 3 (6), E170 (2005)
PUBMED     15869325
REFERENCE  2 (bases 1 to 6195)
AUTHORS    Nielsen,R., Bustamante,C., Clark,A.G., Glanowski,S., Sackton,T.B.,
            Hubisz,M.J., Fledel-Alon,A., Tanenbaum,D.M., Civello,D.,
            White,T.J., Sninsky,J.J., Adams,M.D. and Cargill,M.
TITLE      Direct Submission
JOURNAL    Submitted (05-MAY-2005) Celera Genomics, 45 West Gude Drive,
            Rockville, MD 20850, USA
COMMENT    This sequence was made by sequencing genomic exons and ordering
            them based on alignment. Translation starts at the beginning of
            alignment.
FEATURES   Location/Qualifiers
            source          1..6195
                               /organism="Homo sapiens"
                               /mol_type="genomic DNA"
                               /db_xref="taxon:9606"
                               /chromosome="13"
            gene            <1..>6195
                               /gene="ZIZIMIN1"
                               /locus_tag="HC15707"
ORIGIN
Query Match      73.8%; Score 3547.4; DB 14; Length 6195;
Best Local Similarity 90.4%; Pred. No. 0;
Matches 3878; Conservative 0; Mismatches 113; Indels 297; Gaps 3;

Qy      1 AGTTTACACCATCACCAAAACCCAGAATTTTATGATGAGATTAAATAGAGTTGCCAC 60
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1977 AGTTTACACCATCACCAAAACCCAGAATTTTATGATGAGATTAAATAGAGTTGCCAC 2036

Qy      61 TCAGCTGCATGAAAGCACCACCTGTTGCTCACATTCTTCCATGTCAGCTGTGACAAC 120
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2037 TCAGCTGCATGAAAGCACCACCTGTTGCTCACATTCTTCCATGTCAGCTGTGACAAC 2096

Qy      121 AAGTAAAGGAAGCACGAAGAAGAGGGATGTCGTTGAAACCAAGTTGGCTACTCCTGGCT 180
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2097 AAGTAAAGGAAGCACGAAGAAGAGGGATGTCGTTGAAACCAAGTTGGCTACTCCTGGCT 2156

Qy      181 TCCCTCCTGAAAGACGGAAGGGTGGTGACAAGCGAGCAGCACATCCCGGTCTCGGCGAA 240
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2157 TCCCTCCTGAAAGACGGAAGGGTGGTGACAAGCGAGCAGCACATCCCGGTCTCGGCGAA 2216

Qy      241 CCTTCCTTCGGGCTATCTTGGCTACCAAGAGCTTGGGATGGGCAGGCATTATGGTCCGGA 300
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2217 CCTTCCTTCGGGCTATCTTGGCTACCAAGAGCTTGGGATGGGCAGGCATTATGGTCCGGA 2276

Qy      301 AATTAAATGGGTAGATGGAGGCAAGCCACTGCTGAAAATTTCCACTCATCTGGTTTCTAC 360
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2277 AATTAAATGGGTAGATGGAGGCAAGCCACTGCTGAAAATTTCCACTCATCTGGTTTCTAC 2336

Qy      361 AGTGATACTCAGGATCAGCATTTACATAATTTTTTCCAGTACTGTCAGAAAACCGAATC 420
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2337 AGTGATACTCAGGATCAGCATTTACATAATTTTTTCCAGTACTGTCAGAAAACCGAATC 2396

Qy      421 TGGAGCCCAAGCCTTAGGAAACGAACCTTGTAAAGTACCTTAAGAGTCTGCATGCGATGGA 480
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||

```

## Appendix B

Db	2397	TGGAGCCCAAGCCTTAGGAAACGAACCTGTAAAGTACCTTAAGAGTCTGCATGCGATGGA	2456
Qy	481	AGGCCACGTGATGATCGCCTTCTTGCCCACTATCCTAAACCAGCTGTTCCGAGTCCTCAC	540
Db	2457	AGGCCACGTGATGATCGCCTTCTTGCCCACTATCCTAAACCAGCTGTTCCGAGTCCTCAC	2516
Qy	541	CAGAGCCACACAGGAAGAAGTCGCGGTTAACGTGACTCGGGTCATTATTCATGTGGTTGC	600
Db	2517	CAGAGCCACACAGGAAGAAGTCGCGGTTAACGTGACTCGGGTCATTATTCATGTGGTTGC	2576
Qy	601	CCAGTGCCATGAGGAAGGATTGGAGAGCCACTTGAGGTCATATGTTAAGTACGCGTATAA	660
Db	2577	CCAGTGCCATGAGGAAGGATTGGAGAGCCACTTGAGGTCATATGTTAAGTACGCGTATAA	2636
Qy	661	GGCTGAGCCATATGTTGCCTCTGAATACAAGACAGTGCATGAAGAACTGACCAAATCCAT	720
Db	2637	GGCTGAGCCATATGTTGCCTCTGAATACAAGACAGTGCATGAAGAACTGACCAAATCCAT	2696
Qy	721	GACCACGATTCTCAAGCCTTCTGCCGATTTCCTCACCAGCAACAACTACTGAGGTACTC	780
Db	2697	GACCACGATTCTCAAGCCTTCTGCCGATTTCCTCACCAGCAACAACTACTGAAGTACTC	2756
Qy	781	ATGGTTTTTCTTTGATGTACTGATCAAATCTATGGCTCAGCATTTGATAGAGAACTCCAA	840
Db	2757	ATGGTTTTTCTTTGATGTACTGATCAAATCTATGGCTCAGCATTTGATAGAGAACTCCAA	2816
Qy	841	AGTTAAGTTGCTGCGAAACCAGAGATTTCTGCATCCTATCATCATGCAGCGGAAACCGT	900
Db	2817	AGTTAAGTTGCTGCGAAACCAGAGATTTCTGCATCCTATCATCATGCAGTGGAACCGT	2876
Qy	901	TGTAAATATGCTGATGCCACACATCACTCAGAAGTTTGGAGATAATCCAGAGGCATCTAA	960
Db	2877	TGTAAATATGCTGATGCCACACATCACTCAGAAGTTTGGAGATAATCCAGAGGCATCTAA	2936
Qy	961	GAACGCGAATCATAGCCTTGCTGTCTTCATCAAGAGATGTTTCACCTTCATGGACAGGGG	1020
Db	2937	GAACGCGAATCATAGCCTTGCTGTCTTCATCAAGAGATGTTTCACCTTCATGGACAGGGG	2996
Qy	1021	CTTTGTCTTCAAGCAGATCAACAACCTACATTAGCTGTTTTGCTCCTGGAGACCCAAAGAC	1080
Db	2997	CTTTGTCTTCAAGCAGATCAACAACCTACATTAGCTGTTTTGCTCCTGGAGACCCAAAGAC	3056
Qy	1081	CCTCTTTGAATACAAGTTTGAATTTCTCCGTGTAGTGTGCAACCATGAACATTATATTCC	1140
Db	3057	CCTCTTTGAATACAAGTTTGAATTTCTCCGTGTAGTGTGCAACCATGAACATTATATTCC	3116
Qy	1141	GTTGAACCTTACCAATGCCATTTGGAAAAGGCAGGATTCAAAGATACCAAGACCTCCAGCT	1200
Db	3117	GTTGAACCTTACCAATGCCATTTGGAAAAGGCAGGATTCAAAGATACCAAGACCTCCAGCT	3176
Qy	1201	TGACTACTCATTAACAGATGAGTTCTGCAGAAACCCTTCTTGGTGGGACTGTTACTGAG	1260
Db	3177	TGACTACTCATTAACAGATGAGTTCTGCAGAAACCCTTCTTGGTGGGACTGTTACTGAG	3236
Qy	1261	GGAGGTGGGGACAGCCCTCCAGGAGTTCCGGGAGGTCCGTCTGATCGCCATCAGTGTGCT	1320
Db	3237	GGAGGTGGGGACAGCCCTCCAGGAGTTCCGGGAGGTCCGTCTGATCGCCATCAGTGTGCT	3296
Qy	1321	CAAGAACCTGCTGATAAAGCATTCTTTTGATGACAGATATGCTTCAAGGAGCCATCAGGC	1380
Db	3297	CAAGAACCTGCTGATAAAGCATTCTTTTGATGACAGATATGCTTCAAGGAGCCATCAGGC	3356
Qy	1381	AAGGATAGCCACCCTCTACCTGCCTCTGTTTGGTCTGCTGATTGAAAACGTCCAGCGGAT	1440
Db	3357	AAGGATAGCCACCCTCTACCTGCCTCTGTTTGGTCTGCTGATTGAAAACGTCCAGCGGAT	3416
Qy	1441	CAATGTGAGGGATGTGTACCCTTCCCTGTGAACGCGGGCATGACCGTGAAGGATGAATC	1500
Db	3417	CAATGTGAGGGATGTGTACCCTTCCCTGTGAACGCGGGCATGACTGTGAAGGATGAATC	3476
Qy	1501	CCTGGCTCTACCAGCTGTGAATCCGCTGGTGACGCCGAGAAAGGAAGCACCCTGGACAA	1560
Db	3477	CCTGGCTCTACCAGCTGTGAATCCGCTGGTGACGCCGAGAAAGGAAGCACCCTGGACAA	3536
Qy	1561	CAGCCTGCACAAGGACCTGCTGGGCGCCATCTCCGGCATTGCTTCTCCATATACAACCTC	1620

## Appendix B

Db	3537	CAGCCTGCACAAGGACCTGCTGGGCGCCATCTCCGGCATTGCTTCTCCATATACAACCTC	3596
Qy	1621	AACTCCAAACATCAACAGTGTGAGAAATGCTGATTGAGAGGATCTCTCATAAGCACAGA	1680
Db	3597	AACTCCAAACATCAACAGTGTGAGAAATGCTGATTGAGAGGATCTCTCATAAGCACAGA	3656
Qy	1681	TTCGGGTAACAGCCTTCCAGAAAGGAATAGTGAGAAGAGCAATTCCCTGGATAAGCACCA	1740
Db	3657	TTCGGGTAACAGCCTTCCAGAAAGGAATAGTGAGAAGAGCAATTCCCTGGATAAGCACCA	3716
Qy	1741	ACAAAGTAGCACATTGGGAAATTCCGTGGTTCGCTGTGATAAACTTGACCAGTCTGAGAT	1800
Db	3717	ACAAAGTAGCACATTGGGAAATTCCGTGGTTCGCTGTGATAAACTTGACCAGTCTGAGAT	3776
Qy	1801	TAAGAGCCTACTGATGTGTTTCCTCTACATCTTAAAGAGCATGTCTGATGATGCTTTGTT	1860
Db	3777	TAAGAGCCTACTGATGTGTTTCCTCTACATCTTAAAGAGCATGTCTGATGATGCTTTGTT	3836
Qy	1861	TACATATTGGAACAAGGCTTCAACATCTGAACTTATGGATTTTTCATAATATCTGAAGT	1920
Db	3837	TACATATTGGAACAAGGCTTCAACATCTGAACTTATGGATTTTTCATAATATCTGAAGT	3896
Qy	1921	CTGCCTGCACCAGTTCCAGTACATGGGGAAGCGATACATAGCCAGGAACCAGAGGGGTT	1980
Db	3897	CTGCCTGCACCAGTTCCAGTACATGGGGAAGCGATACATAGC-----	3938
Qy	1981	GGGACCCATAGTTTCATGATCGAAAGTCTCAGACATTGCCTGTTTCCCGTAACAGAACAGG	2040
Db	3939	-----CAGAACAGG	3947
Qy	2041	AATGATGCATGCCAGATTGCAGCAGCTGGGCAGCCTGGATAACTCTCTCACTTTTAACCA	2100
Db	3948	AATGATGCATGCCAGATTGCAGCAGCTGGGCAGCCTGGATAACTCTCTCACTTTTAACCA	4007
Qy	2101	CAGCTATGGCCACTCGGACGCAGATGTTCTGCACCAGTCATTACTTGAAGCCAACATTGC	2160
Db	4008	CAGCTATGGCCACTCGGACGCAGATGTTCTGCACCAGTCATTACTTGAAGCCAACATTGC	4067
Qy	2161	TACTGAGGTTTGCCTGACAGCTCTGGACACGCTTTCTCTATTACATTGGCGTTTAAGAA	2220
Db	4068	TACTGAGGTTTGCCTGACAGCTCTGGACACGCTTTCTCTATTACATTGGCGTTTAAGAA	4127
Qy	2221	CCAGCTCCTGGCCGACCATGGACATAATCCTCTCATGAAAAAGTTTGTGATGTCTACCT	2280
Db	4128	CCAGCTCCTGGCCGACCATGGACATAATCCTCTCATGAAAAAGTTTGTGATGTCTACCT	4187
Qy	2281	GTGTTTTCTTCAAAAACATCAGTCTGAAACGGCTTTAAAAAATGTCTTCACTGCCTTAAG	2340
Db	4188	GTGTTTTCTTCAAAAACATCAGTCTGAAACGGCTTTAAAAAATGTCTTCACTGCCTTAAG	4247
Qy	2341	GTCCTTAATTTATAAGTTTCCCTCAACATTCTATGAAGGGAGAGCGGACATGTGTGCGGC	2400
Db	4248	GTCCTTAATTTATAAGTTTCCCTCAACATTCTATGAAGGGAGAGCGGACATGTGTGCGGC	4307
Qy	2401	TCTGTGTTACGAGATTCTCAAGTGCTGTAACCCAAGCTGAGCTCCATCAGGACGGAGGC	2460
Db	4308	TCTGTGTTACGAGATTCTCAAGTGCTGTAACCCAAGCTGAGCTCCATCAGGACGGAGGC	4367
Qy	2461	CTCCCAGCTGCTCTACTTCTCTGATGAGGAACAACCTTTGATTACACTGGAAAGAAGTCCTT	2520
Db	4368	CTCCCAGCTGCTCTACTTCTCTGATGAGGAACAACCTTTGATTACACTGGAAAGAAGTCCTT	4427
Qy	2521	TGTCCGGACACATTTGCAAGTCATCATATCTGTGAGCCAGCTGATAGCAGACGTTGTTGG	2580
Db	4428	TGTCCGGACACATTTGCAAGTCATCATATCTGTGAGCCAGCTGATAGCAGACGTTGTTGG	4487
Qy	2581	CATTGGGGAAACCAGATTCCAGCAGTCCCTGTCCATCATCAACAACTGTGCCAACAGTGA	2640
Db	4488	CATTGGGGAAACCAGATTCCAGCAGTCCCTGTCCATCATCAACAACTGTGCCAACAGTGA	4547
Qy	2641	CCGGCTTATTAAGCACACCAGCTTCTCCTCTGATGTGAAGGACTTAACCAAAGGATACG	2700
Db	4548	CCGGCTTATTAAGCACACCAGCTTCTCCTCTGATGTGAAGGACTTAACCAAAGGATACG	4607
Qy	2701	CACGGTGCTAATGGCCACCGCCAGATGAAGGAGCATGAGAACGACCCAGAGATGCTGGT	2760



## Appendix B

```

Db      4608 CACGGTGCTAATGGCCACCGCCAGATGAAGGAGCATGAGAACGACCCAGAGATGCTGGT 4667
Qy      2761 GGACCTCCAGTACAGCCTGGCCAAATCCTATGCCAGCACGCCCGAGCTCAGGAAGACGTG 2820
      |||
Db      4668 GGACCTCCAGTACAGCCTGGCCAAATCCTATGCCAGCACGCCCGAGCTCAGGAAGACGTG 4727
Qy      2821 GCTCGACAGCATGGCCAGGATCCATGTCAAAAATGGCGATCTCTCAGAGGCAGCAATGTG 2880
      |||
Db      4728 GCTCGACAGCATGGCCAGGATCCATGTCAAAAATGGCGATCTCTCAGAGGCAGCAATGTG 4787
Qy      2881 CTATGTCCACGTAACAGCCCTAGTGGCAGAATATCTCACACGGAA----- 2925
      |||
Db      4788 CTATGTCCACGTAACAGCCCTAGTGGCAGAATATCTCACACGGAAAGAAGCAGTCCAGTG 4847
Qy      2926 -----AGGCGT 2931
      ||
Db      4848 GGAGCCGCCCCCTTCTCCCCACAGCCATAGCGCCTGCCTGAGGAGGAGCCGGGGAGNNNN 4907
Qy      2932 GTTTAGACAAGGATGCACCGCCTTCAGGGTCATTACCCCAAACATCGACGAGGAGGCCTC 2991
Db      4908 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN 4967
Qy      2992 CATGATGGAAGACGTGGGGATGCAGGATGTCCATTTCAACGAGGATGTGCTGATGGAGCT 3051
      |||
Db      4968 NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNGATGTGCTGATGGAGCT 5027
Qy      3052 CCTTGAGCAGTGCAGCATGGACTCTGGAAGCCGAGCGCTACGAGCTCATCGCCGACAT 3111
      |||
Db      5028 CCTTGAGCAGTGCAGCATGGACTCTGGAAGCCGAGCGCTACGAGCTCATCGCCGACAT 5087
Qy      3112 CTACAAACTTATCATCCCCATTTATGAGAAGCGGAGGGAT----- 3151
      |||
Db      5088 CTACAAACTTATCATCCCCATTTATGAGAAGCGGAGGGATTTTGAAGGCTGGCCCATCT 5147
Qy      3152 ----- 3151
Db      5148 GTATGACACGCTGCACCGGGCTACAGCAAAGTGACCGAGGTCATGCACTCGGGCCGAG 5207
Qy      3152 ----- 3151
Db      5208 GCTTCTGGGGACCTACTTCCGGGTAGCCTTCTTCGGGCAGCAATACCAGTTTACAGACAG 5267
Qy      3152 -----TTCTTTGAAGATGAAGATGGAAGGAGTATATTTACAAGGA 3192
      |||
Db      5268 TGAACAGATGTGGAGGGATTCTTTGAAGATGAAGATGGAAGGAGTATATTTACAAGGA 5327
Qy      3193 ACCCAAACACACCGCTGTTCGGAATTTCTCAGAGACTCCTTAAACTGTACTCGGATAA 3252
      |||
Db      5328 ACCCAAACACACCGCTGTTCGGAATTTCTCAGAGACTCCTTAAACTGTACTCGGATAA 5387
Qy      3253 ATTTGGTTCTGAAAATGTCAAAATGATACAGGATTCTGGCAAGGTCAACCTAAGGATCT 3312
      |||
Db      5388 ATTTGGTTCTGAAAATGTCAAAATGATACAGGATTCTGGCAAGGTCAACCTAAGGATCT 5447
Qy      3313 GGATTCTAAGTATGCATACATCCAGGTGACTCACGTCATCCCCTTCTTTGACGAAAAGA 3372
      |||
Db      5448 GGATTCTAAGTATGCATACATCCAGGTGACTCACGTCATCCCCTTCTTTGACGAAAAGA 5507
Qy      3373 GTTGCAAGAAAGGAAAACAGAGTTTGAGAGATCCCACAACATCCGCCGCTTCATGTTGA 3432
      |||
Db      5508 GTTGCAAGAAAGGAAAACAGAGTTTGAGAGATCCCACAACATCCGCCGCTTCATGTTGA 5567
Qy      3433 GATGCCATTTACGCAGACCGGGAAGAGGCAGGGCGGGTGAAGAGCAGTGCAAACGGCG 3492
      |||
Db      5568 GATGCCATTTACGCAGACCGGGAAGAGGCAGGGCGGGTGAAGAGCAGTGCAAACGGCG 5627
Qy      3493 CACCATCTGACAGCCATACACTGCTTCCCTTATGTGAAGAAGCGCATCCCTGTCATGTA 3552
      |||
Db      5628 CACCATCTGACAGCCATACACTGCTTCCCTTATGTGAAGAAGCGCATCCCTGTCATGTA 5687
Qy      3553 CCAGCACCACACTGACCTGAACCCCATCGAGGTGGCCATTGACGAGATGAGTAAGAAGGT 3612
      |||
Db      5688 CCAGCACCACACTGACCTGAACCCCATCGAGGTGGCCATTGACGAGATGAGTAAGAAGGT 5747
Qy      3613 GGCGGAGCTCCGGCAGCTGTGCTCCTCGGCCGAGGTGGACATGATCAAACGCACTCAA 3672
      |||

```

## Appendix B

```
Db      5748 GGC GGAGCTCCGGCAGCTGTGCTCCTCGGCCGAGGTGGACATGATCAAAGTGCAGCTCAA 5807
Qy      3673 ACTCCAGGGCAGCGTGAGTGTTTCAGGTCAATGCTGGCCCACTAGCATATGCGCGAGCTTT 3732
      |||
Db      5808 ACTCCAGGGCAGCGTGAGTGTTTCAGGTCAATGCTGGCCCACTAGCATATGCGCGAGCTTT 5867
Qy      3733 CTTAGATGATACAAACACAAAGCGATATCCTGACAATAAAGTGAAGCTGCTTAAGGAAGT 3792
      |||
Db      5868 CTTAGATGATACAAACACAAAGCGATATCCTGACAATAAAGTGAAGCTGCTTAAGGAAGT 5927
Qy      3793 TTTCAGGCAATTTGTGGAAGCTTGCGGTCAAGCCTTAGCGGTAAACGAACGTCTGATTAA 3852
      |||
Db      5928 TTTCAGGCAATTTGTGGAAGCTTGCGGTCAAGCCTTAGCGGTAAACGAACGTCTGATTAA 5987
Qy      3853 AGAAGACCAGCTCGAGTATCAGGAAGAAATGAAAGCCAACTACAGGGAATGGCGAAGGA 3912
      |||
Db      5988 AGAAGACCAGCTCGAGTATCAGGAAGAAATGAAAGCCAACTACAGGGAATGGCGAAGGA 6047
Qy      3913 GCTTTCTGAAATCATGCATGAGCAGATCTGCCCCCTGGAGGAGAAGACGAGCGTCTTACC 3972
      |||
Db      6048 GCTTTCTGAAATCATGCATGAGCAGATCTGCCCCCTGGAGGAGAAGACGAGCGTCTTACC 6107
Qy      3973 GAATTCCTTTCACATCTTCAACGCCATCAGTGGGACTCCAACAAGCACAATGGTTCACGG 4032
      |||
Db      6108 GAATTCCTTTCACATCTTCAACGCCATCAGTGGGACTCCAACAAGCACAATGGTTCACGG 6167
Qy      4033 GATGACCAGCTCGTCTTCGGTCGTGTGA 4060
      |||
Db      6168 GATGACCAGCTCGTCTTCGGTCGTGTGA 6195
<!--EndFragment-->
```